

Appln. No. 09/711,896
Amd. dated March 28, 2005
Reply to Office Action of September 9, 2004

REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claims are allowed. Claims 1, 4, 6-25, and 27 presently appear in this application, with claims 10-23 withdrawn from consideration by the examiner, and define patentable subject matter warranting their allowance. It is noted that rejoinder of non-elected claims which fall within the allowable genus has been earlier requested if a generic claim is found to be allowable. Reconsideration and allowance are hereby respectfully solicited.

Claim 1 and claims dependent therefrom have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is obviated by the amendment to claim 1.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 1, 4-9, 24 and 25 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is obviated by the amendment to the claims.

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Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 4-6, 24 and 25 have been rejected under 35 U.S.C. §102(b) as being anticipated by Akita et al., *J. Biol. Chem.* 272:26595-26603 (1997). This rejection is respectfully traversed.

Applicants believe that the antibody recited in claim 1 is specific for the leader sequence in the IL-18 precursor, which leader sequence is not present in the mature IL-18 polypeptide. Support for the recitation that the antibody does not recognize mature human interleukin-18 is found on page 32, first full paragraph (middle of page). By contrast, Akita discloses an anti-hIL-18 antibody which was raised against the mature recombinant IL-18 protein (see page 26595, right column, in "Reagents and Antibodies" section). Thus, the antibody disclosed by Akita recognizes both the IL-18 precursor and the mature IL-18 because it was obtained by using a partial sequence of mature IL-18. Applicants point out that the presently claimed antibody only recognizes the IL-18 precursor and not the mature IL-18. Accordingly, Akita does not anticipate the claims as amended.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

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Claim 9 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Akita et al. as applied to claim 1 above. This rejection is respectfully traversed.

Claim 9 is dependent from claim 1. As the antibody of claim 1 is not anticipated by Akita, an immunoassay kit in which the antibody only recognizes the IL-18 precursor but not the mature IL-18 cannot be made obvious from the disclosures and teachings of Akita.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

The rejection of claim 1, 4-8 and 24 made in paragraph 23 of the Office Action mailed January 21, 2004, and the rejection of claims 9 and 25 made in paragraph 24 of the same Office Action under 35 U.S.C. §103(a) as being unpatentable over Yong et al. in view of Campbell et al. are maintained. The rejections are respectfully traversed.

While Yong discloses the IL-18 precursor and the preparation of IL-18 precursor protein and mature IL-18 from *E. coli*, applicants submit that Yong does not disclose or teach an antibody that recognizes the IL-18 precursor, i.e., the leader sequence, but which does not recognize the mature IL-18 protein.

One of ordinary skill in the art may obtain antibodies which recognize the IL-18 precursor if such a

person uses the recombinant IL-18 precursor disclosed by Yong as an antigen and follows Campbell's teaching. However, it should be pointed out that many of the thus obtained antibodies also would recognize the mature IL-18 protein. It would then become necessary to select antibodies that do not recognize the mature IL-18 protein from among the many antibodies obtained in order to arrive at an antibody as claimed in the amended claim 1. The Campbell reference does not teach such selection. Furthermore, it should be noted that neither Yong nor Campbell suggests preparation of an antibody that recognizes only the precursor of a protein, such as IL-18, by using the leader sequence of a protein.

As disclosed in the present specification at page 2, line 7 to page 3, line 7, IL-18 exists in both the mature form and the precursor form. However, the IL-18 precursor has no IL-18 activity; it is only IL-18 in the mature form that reveals IL-18 activity. Nevertheless, an antibody which is obtained by using mature IL-18 as antigen recognizes the IL-18 precursor as well as mature IL-18. In this regard, such an antibody obtained by using mature IL-18 as antigen cannot be used to accurately measure IL-18 activity, whereas it can be used to measure the amount of total IL-18 (precursor and mature forms). The present inventors have succeeded in obtaining an antibody that recognizes only the IL-18 precursor

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and have made it possible to measure the amount of IL-18 having no IL-18 activity. As a result of the present invention, it is now possible to accurately measure IL-18 activity by using conventional antibodies in combination with an antibody of the presently claimed invention. Neither Yong nor Campbell teaches this. Accordingly, Yong and Campbell cannot lead one of ordinary skill in the art to the presently claimed invention.

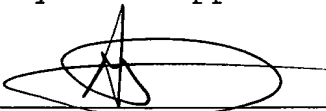
Reconsideration and withdrawal of the §103(a) rejections are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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